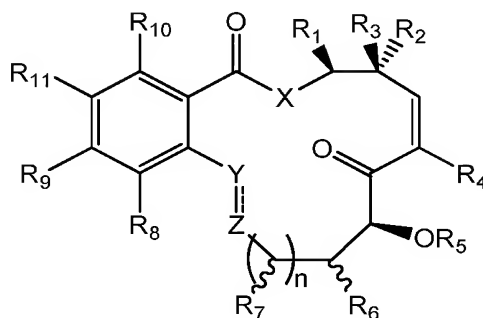


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listing of claims in the application.

Listing of Claims

1. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester thereof; wherein

R₁ is hydrogen, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀ heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀ heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl or C₃-C₁₄ heteroaryl;

R₂ is ~~C₁₋₆-alkyl~~ methyl;

R₃ is hydrogen, ~~or halogen, hydroxyl, protected hydroxyl, or a C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀ heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀ heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl or C₃-C₁₄ heteroaryl moiety; or~~

~~R₁ and R₃, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;~~

R₄ is hydrogen or halogen;

R₅ is hydrogen or an oxygen protecting group;

R₆ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

~~R₇, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;~~
 R₈ is hydrogen, halogen, hydroxyl, protected hydroxyl, or alkyloxy, ~~or a C₁-C₂₀ alkyl,~~
~~C₂-C₂₀ alkenyl or C₂-C₂₀ alkynyl moiety optionally substituted with hydroxyl, protected~~
~~hydroxyl, SR₁₂, or NR₁₂R₁₃;~~

R₉ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR₁₂, SR₁₂, NR₁₂R₁₃,
 -X₁(CH₂)_pX₂-R₁₄, or is lower alkyl optionally substituted with hydroxyl, protected
 hydroxyl, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;

wherein R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, C₁-C₂₀ alkyl,
 C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀
 heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀
 heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl
 or C₃-C₁₄ heteroaryl; or a nitrogen or oxygen protecting group, or R₁₂ and R₁₃, taken
 together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1
 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further
 substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy,
 amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X₁ and X₂ are each independently absent, or are oxygen, NH, or
 -N(alkyl), or wherein X₂-R₁₄ together are N₃ or are a saturated or unsaturated
 heterocyclic moiety[[,]] ;

p is 2-10, and

R₁₄ is hydrogen, or a C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, C₁-C₂₀ alkyl(C₃-C₁₄)aryl, or C₁-
 C₂₀ alkyl(C₃-C₁₄)heteroaryl moiety, or is -(C=O)NHR₁₅, -(C=O)OR₁₅, or -(C=O)R₁₅,
 wherein each occurrence of R₁₅ is independently hydrogen, C₁-C₂₀ alkyl, C₂-C₂₀
 alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀
 heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀
 heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl
 or C₃-C₁₄ heteroaryl; or R₁₄ is -SO₂(R₁₆), wherein R₁₆ is a C₁-C₂₀ alkyl, C₂-C₂₀
 alkenyl or C₂-C₂₀ alkynyl moiety, wherein one or more of R₁₄, R₁₅, or R₁₆ are
 optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl,
 alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R₈ and R₉ may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4
 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with

hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R₁₀ is ~~hydrogen~~, hydroxyl, protected hydroxyl, or amino, ~~or protected amino~~;

R₁₁ is hydrogen, ~~hydroxyl or protected hydroxyl~~;

X is O;

Y is CHR₁₇[[, C=O,]] or CR₁₇; and Z is CHR₁₈[[, C=O,]] or CR₁₈[[,]] ;

wherein each occurrence of R₁₇ and R₁₈ is ~~independently~~ hydrogen, ~~C₁-C₂₀-alkyl, C₂-C₂₀-alkenyl or C₂-C₂₀-alkynyl~~ and wherein Y and Z may be connected by a single or double bond;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

wherein C₃-C₁₄ heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

2. (currently amended) The composition of claim 1, wherein:

R₁ is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C₃-C₁₄ aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

~~R₂ is methyl;~~

R₃ is hydrogen, ~~halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C₃-C₁₄-aryl,~~

~~wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or~~

~~R₄ and R₃, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;~~

~~R₄ is hydrogen or halogen;~~

~~R₅ is hydrogen or a protecting group;~~

~~R₆ is hydrogen, hydroxyl, or protected hydroxyl;~~

~~n is 0-2;~~

~~R₇, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;~~

~~R₈ is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR₁₂, or NR₁₂R₁₃;~~

~~R₉ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR₁₂, SR₁₂, NR₁₂R₁₃, -X₁(CH₂)_pX₂-R₁₄, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;~~

wherein R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, lower alkyl, C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl, or a nitrogen or oxygen protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X₁ and X₂ are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X₂-R₁₄ together are N₃ or are a saturated or unsaturated heterocyclic moiety, p is 2-10, and

R₁₄ is hydrogen, or a C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl moiety, or is -(C=O)NHR₁₅, -(C=O)OR₁₅, or -(C=O)R₁₅, wherein each occurrence of R₁₅ is independently hydrogen, alkyl, heteroalkyl, C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl, or R₁₄ is -SO₂(R₁₆), wherein R₁₆ is an alkyl moiety, wherein one or more of R₁₄, R₁₅, or R₁₆ are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

~~R₈ and R₉ may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with~~

~~hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; and~~

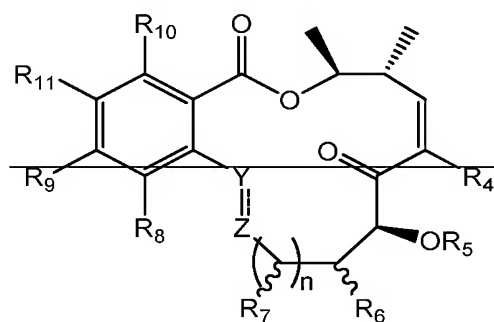
~~R₁₀ is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;~~

~~R₁₁ is hydrogen, hydroxyl or protected hydroxyl;~~

~~X is O;~~

~~Y is CHR₁₇, C=O, or CR₁₇; and Z is CHR₁₈, C=O, or CR₁₈, wherein each occurrence of R₁₇ and R₁₈ is independently hydrogen or lower alkyl, wherein Y and Z may be connected by a single or double bond.~~

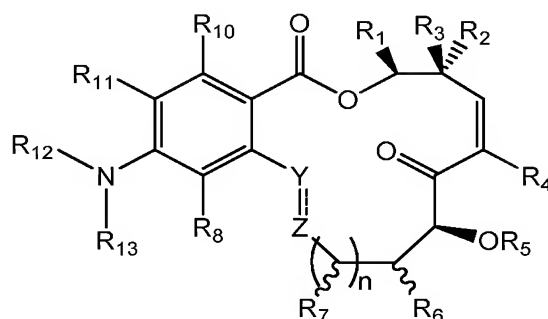
3. (currently amended) The composition of claim 2, where ~~and~~ n is 1.
4. (original) The composition of claim 2, where R₄ is halogen.
5. (original) The composition of claim 2, where R₄ is fluorine.
6. (original) The composition of claim 2, where Y and Z together represent -CH=CH-.
7. (original) The composition of claim 2, where Y and Z together represent trans -CH=CH-.
8. (currently amended) The composition of claim 2, wherein R₁ is ~~and R₂ are each~~ methyl ~~and R₃ is hydrogen and the compound has the structure:~~



~~wherein R₄, R₁₁, n, Y and Z are as defined in claim 2.~~

9. (previously presented) The composition of claim 8, wherein n is 1.
10. (original) The composition of claim 8, wherein R₄ is halogen.

11. (original) The composition of claim 8, wherein Y and Z together represent $-\text{CH}=\text{CH}-$.
12. (previously presented) The composition of claim 8, wherein n is 1, R_4 is halogen and Y and Z together represent $-\text{CH}=\text{CH}-$.
13. (original) The composition of claim 11 or 12 wherein $-\text{CH}=\text{CH}-$ is trans.
14. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester thereof; wherein

R_1 is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or $\text{C}_3\text{-C}_{14}$ aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R_2 is C_{1-6} -alkyl methyl;

R_3 is hydrogen[,], or halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or $\text{C}_3\text{-C}_{14}$ aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R_1 and R_3 , when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R_4 is hydrogen or halogen;

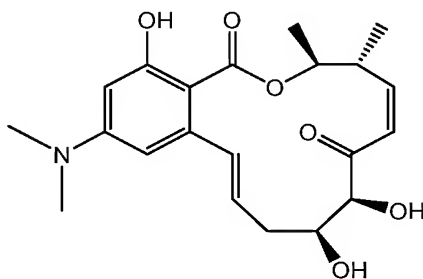
R_5 is hydrogen or [[a]] an oxygen protecting group;

R_6 is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

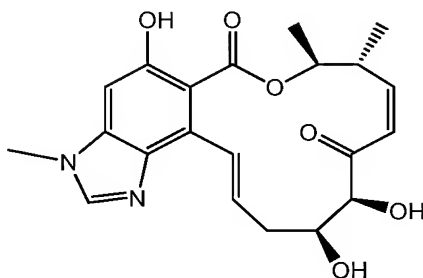
~~R₇, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;~~
R₈ is hydrogen, halogen, hydroxyl, protected hydroxyl, or alkyloxy, ~~or lower alkyl~~
~~optionally substituted with hydroxyl, protected hydroxyl, SR₁₂, or NR₁₂R₁₃;~~
R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, lower alkyl, C₃-C₁₄ aryl,
C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl, or a nitrogen or oxygen
protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated
cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂
and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl,
protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or
halogen[[,]];
R₁₀ is ~~hydrogen,~~ hydroxyl, protected hydroxyl, or amino, ~~or protected amino;~~
R₁₁ is hydrogen, ~~hydroxyl or protected hydroxyl;~~
~~X is O;~~
Y is CHR₁₇[[, C=O,]] or CR₁₇; and Z is CHR₁₈[[, C=O,]] or CR₁₈[[,]];
wherein each occurrence of R₁₇ and R₁₈ is ~~independently~~ hydrogen ~~or lower alkyl,~~
wherein Y and Z may be connected by a single or double bond, or
R₁₃ and R₈ may, when taken together, form a cyclic ring of 1 to 4 carbon atoms and 1 to
3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino,
alkylamino, aminoalkyl, and halogen;
wherein oxygen protecting groups are selected from the group consisting of methyl
ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-
methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl
ether, triethylsilylether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl
ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate,
dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting
groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides,
N-alkyl amines, N-aryl amines, imines, and enamines; and
wherein C₃-C₁₄ heteroaryl moieties are selected from cyclic aromatic moieties having
from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one
or two ring atoms are additional heteroatoms independently selected from S, O and N;
and the remaining ring atoms are carbon.

15. (previously presented) The composition of claim 14, wherein n is 1.
16. (original) The composition of claim 14, wherein R₄ is halogen.
17. (original) The composition of claim 14, wherein Y and Z together represent -CH=CH-.
18. (currently amended) The composition of claim 14, wherein R₁ is and ~~R₂ are each~~ methyl and ~~R₃ is hydrogen~~.
19. (currently amended) The composition of claim 14, wherein n is 1, R₁ is and ~~R₂ are each~~ methyl, ~~R₃ is hydrogen~~, R₄ is halogen, and Y and Z together represent -CH=CH-.
20. (original) The composition of claim 17 or 19, wherein -CH=CH- is trans.
- 21-22. (canceled)
23. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

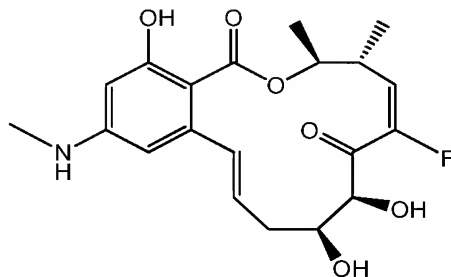
24. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

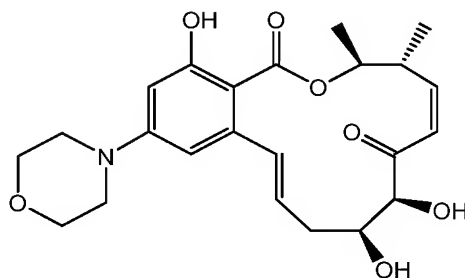
25-26. (canceled)

27. (previously presented) The composition of claim 14, wherein the compound has the structure:



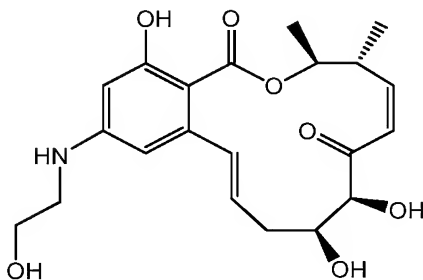
or a pharmaceutically acceptable salt or ester thereof.

28. (previously presented) The composition of claim 14, wherein the compound has the structure:



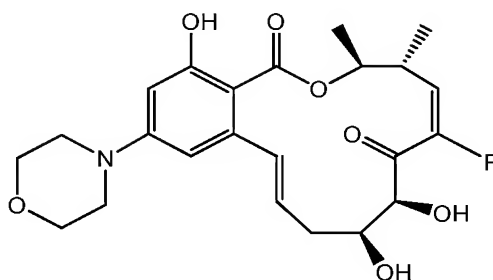
or a pharmaceutically acceptable salt or ester thereof.

29. (previously presented) The composition of claim 14, wherein the compound has the structure:



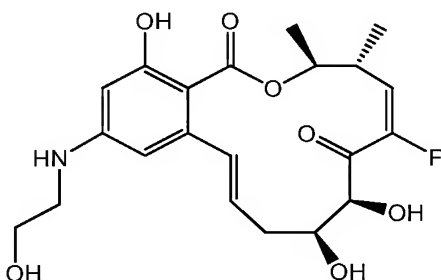
or a pharmaceutically acceptable salt or ester thereof.

30. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

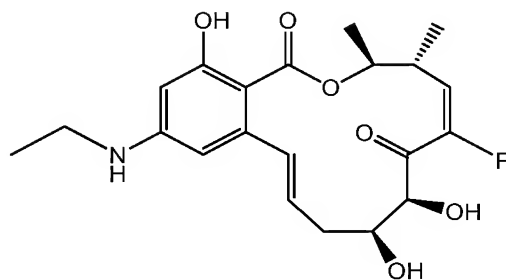
31. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

32. (canceled)

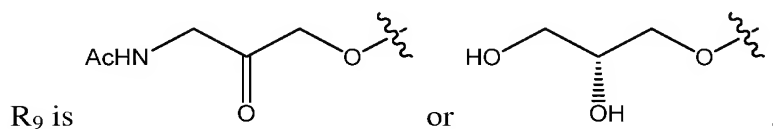
33. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

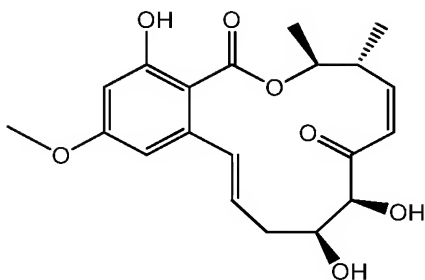
- 34-45. (canceled)

46. (withdrawn, currently amended) The composition of claim 2, where R_1 is hydrogen ~~or methyl~~.
47. (withdrawn, currently amended) The composition of claim ~~[[2]]~~ 1, where R_3 is ~~hydrogen or~~ halogen.
48. (withdrawn) The composition of claim 2, where R_4 is hydrogen.
49. (withdrawn) The composition of claim 2, where R_5 is hydrogen.
50. (withdrawn) The composition of claim 2, where R_6 is hydroxyl.
51. (canceled)
52. (withdrawn, currently amended) The composition of claim ~~[[2]]~~ 1, where R_8 is ~~hydrogen or~~ halogen.
53. (withdrawn) The composition of claim 2, where R_9 is hydroxyl, protected hydroxyl, $-OR_{12}$, $-NR_{12}R_{13}$, or $-O(CH_2)_pX_2-R_{14}$, wherein R_{12} , R_{13} , R_{14} and X_2 are as defined in claim 2.
54. (withdrawn, currently amended) The composition of claim 53, where R_9 is $-OR_{12}$, wherein R_{12} is methyl, ethyl, propyl, isopropyl, butyl, ~~$-CH_2COOMe$~~ , Bn, PMB (MPM), 3,4-ClBn, or



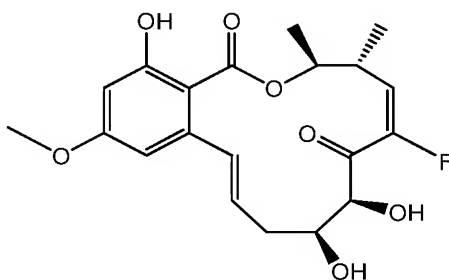
55.-61. (canceled)

62. (previously presented) The composition of claim 1 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

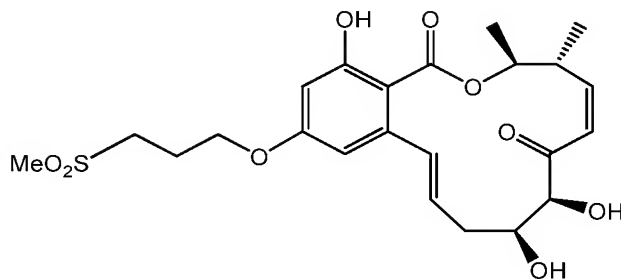
63. (previously presented) The composition of claim 1 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

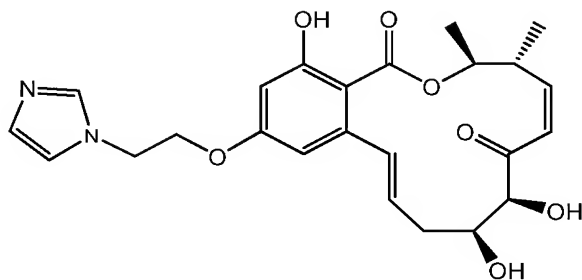
64. (canceled)

65. (previously presented) The composition of claim 1 wherein the compound has the structure:



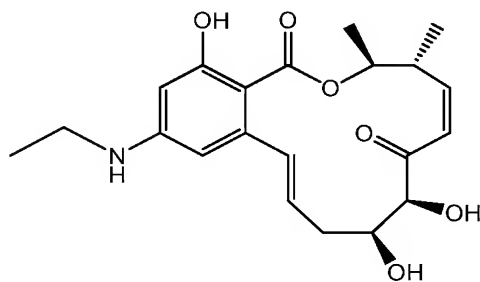
or a pharmaceutically acceptable salt or ester thereof.

66. (previously presented) The composition of claim 1 wherein the compound has the structure:



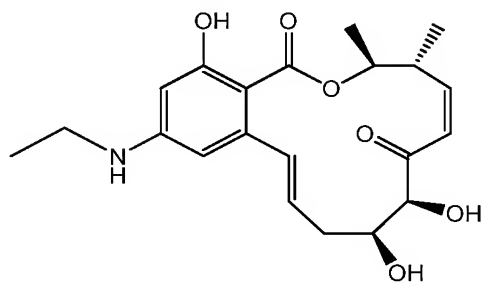
or a pharmaceutically acceptable salt or ester thereof.

67. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:

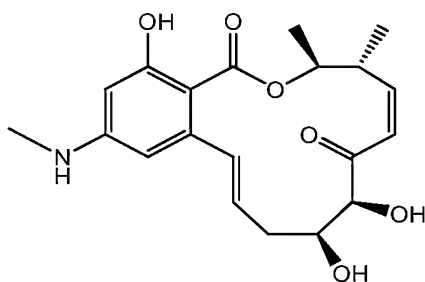


or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

68. (new) The composition of claim 67, having the structure:

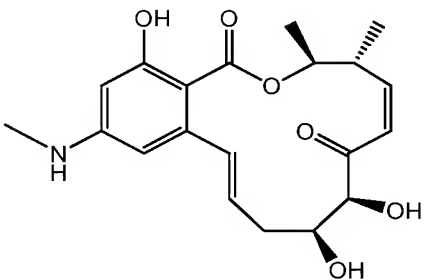


69. (new) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:

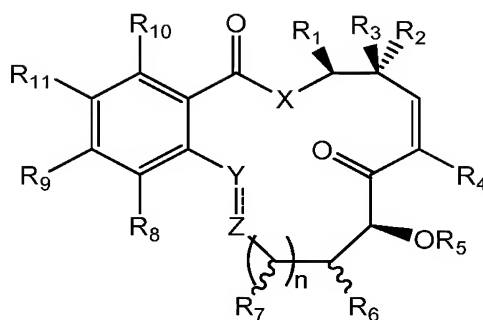


or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

70. (new) The composition of claim 69, having the structure:



71. (new) The composition of claim 2, wherein R_4 , R_5 and R_8 are hydrogen, R_6 and R_{10} are hydroxyl, and Y and Z together represent trans -CH=CH-.
72. (new) The composition of claim 71, wherein R_1 is methyl.
73. (new) The composition of claim 14, wherein R_4 , R_5 and R_8 are hydrogen, R_6 and R_{10} are hydroxyl, and Y and Z together represent trans -CH=CH-.
74. (new) The composition of claim 73, wherein R_1 is methyl.
75. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester or salt of ester thereof; wherein

R₁ is hydrogen, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀ heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀ heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl or C₃-C₁₄ heteroaryl;

R₂ is methyl;

R₃ is hydrogen or halogen;

R₄ is hydrogen or halogen;

R₅ is hydrogen or an oxygen protecting group;

R₆ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R₇ is hydrogen;

R₈ is hydrogen, halogen, hydroxyl, protected hydroxyl, or alkyloxy;

R₉ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR₁₂, SR₁₂, NR₁₂R₁₃,

-X₁(CH₂)_pX₂-R₁₄, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;

wherein R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀ heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀ heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl or C₃-C₁₄ heteroaryl; or a nitrogen or oxygen protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2 - R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety;

p is 2-10, and

R_{14} is hydrogen or a C_3 - C_{14} aryl, C_3 - C_{14} heteroaryl, C_1 - C_{20} alkyl(C_3 - C_{14})aryl, or C_1 - C_{20} alkyl(C_3 - C_{14})heteroaryl moiety, or is $-(C=O)NHR_{15}$, $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, C_2 - C_{20} alkynyl, C_1 - C_{20} heteroalkyl, C_2 - C_{20} heteroalkenyl, C_2 - C_{20} heteroalkynyl, C_3 - C_{20} cycloalkyl, C_3 - C_{20} cycloalkenyl, C_3 - C_{20} cycloalkynyl, C_3 - C_{20} heterocycloalkyl, C_3 - C_{20} heterocycloalkenyl, C_3 - C_{20} heterocycloalkynyl, C_3 - C_{14} aryl or C_3 - C_{14} heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is a C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl or C_2 - C_{20} alkynyl moiety, wherein one or more of R_{14} , R_{15} , or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydroxyl, protected hydroxyl, or amino;

R_{11} is hydrogen;

X is O;

Y is CHR_{17} or CR_{17} ; and Z is CHR_{18} or CR_{18} ;

wherein each occurrence of R_{17} and R_{18} is hydrogen and wherein Y and Z may be connected by a single or double bond;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyl dimethylsilyl ether, tribenzyl silyl ether, t-butyl diphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

wherein C₃-C₁₄ heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

76. (new) The composition of claim 75, wherein:

R₁ is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C₃-C₁₄ aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R₃ is hydrogen;

R₈ is hydrogen;

R₉ is hydrogen, halogen, hydroxyl, protected hydroxyl, OR₁₂, SR₁₂, NR₁₂R₁₃,

-X₁(CH₂)_pX₂-R₁₄, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;

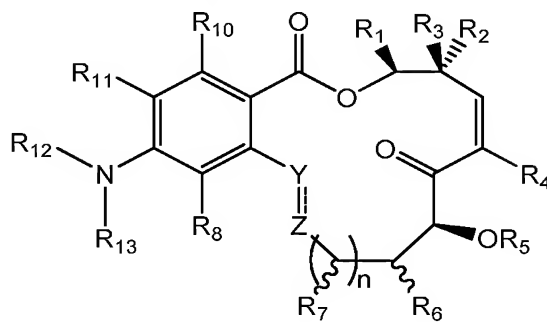
wherein R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, lower alkyl, C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl, or a nitrogen or oxygen protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X₁ and X₂ are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X₂-R₁₄ together are N₃ or are a saturated or unsaturated heterocyclic moiety, p is 2-10, and

R₁₄ is hydrogen, or a C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl moiety, or is -(C=O)NHR₁₅, -(C=O)OR₁₅, or -(C=O)R₁₅, wherein each occurrence of R₁₅ is independently hydrogen, alkyl, heteroalkyl, C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl, or R₁₄ is -SO₂(R₁₆), wherein R₁₆ is an alkyl moiety, wherein one or more of R₁₄, R₁₅, or R₁₆ are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; and

R₁₀ is hydroxyl.

77. (new) The composition of claim 76, where n is 1.
78. (new) The composition of claim 76, where R₄ is halogen.
79. (new) The composition of claim 76, where R₄ is fluorine.
80. (new) The composition of claim 76, where Y and Z together represent -CH=CH-.
81. (new) The composition of claim 76, where Y and Z together represent trans -CH=CH-.
82. (new) The composition of claim 76, wherein R₁ is methyl.
83. (new) The composition of claim 82, wherein n is 1.
84. (new) The composition of claim 82, wherein R₄ is halogen.
85. (new) The composition of claim 82, wherein Y and Z together represent -CH=CH-.
86. (new) The composition of claim 82, wherein n is 1, R₄ is halogen and Y and Z together represent -CH=CH-.
87. (new) The composition of claim 85 or 86 wherein -CH=CH- is trans.
88. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester or salt of ester thereof; wherein

R₁ is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C₃-C₁₄ aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R₂ is methyl;

R₃ is hydrogen or halogen;

R₄ is hydrogen or halogen;

R₅ is hydrogen or an oxygen protecting group;

R₆ is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R₇ is hydrogen;

R₈ is hydrogen, halogen, hydroxyl, protected hydroxyl, or alkyloxy;

R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, lower alkyl, C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl, or a nitrogen or oxygen protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R₁₀ is hydroxyl, protected hydroxyl, or amino;

R₁₁ is hydrogen;

Y is CHR₁₇ or CR₁₇; and Z is CHR₁₈ or CR₁₈;

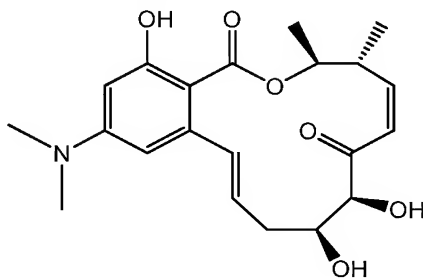
wherein each occurrence of R₁₇ and R₁₈ is hydrogen, wherein Y and Z may be connected by a single or double bond, or

R₁₃ and R₈ may, when taken together, form a cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl

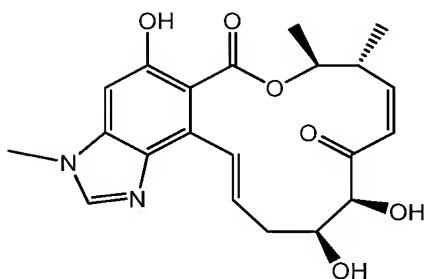
ether, t-butyl diphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and wherein C₃-C₁₄ heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

89. (new) The composition of claim 88, wherein n is 1.
90. (new) The composition of claim 88, wherein R₄ is halogen.
91. (new) The composition of claim 88, wherein Y and Z together represent -CH=CH-.
92. (new) The composition of claim 88, wherein R₁ is methyl.
93. (new) The composition of claim 88, wherein n is 1, R₁ is methyl, R₄ is halogen, and Y and Z together represent -CH=CH-.
94. (new) The composition of claim 91 or 93, wherein -CH=CH- is trans.
95. (new) The composition of claim 88, wherein the compound has the structure:



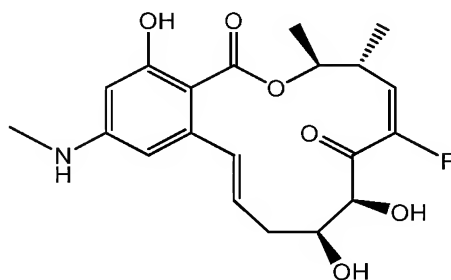
or a pharmaceutically acceptable salt or ester thereof.

96. (new) The composition of claim 88, wherein the compound has the structure:



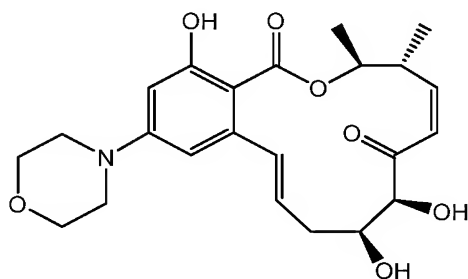
or a pharmaceutically acceptable salt or ester thereof.

97. (new) The composition of claim 88, wherein the compound has the structure:



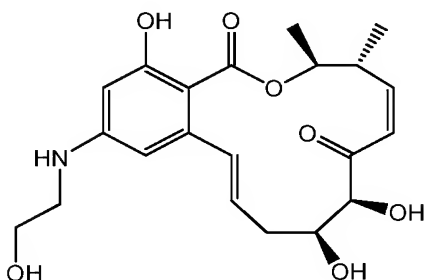
or a pharmaceutically acceptable salt or ester thereof.

98. (new) The composition of claim 88, wherein the compound has the structure:



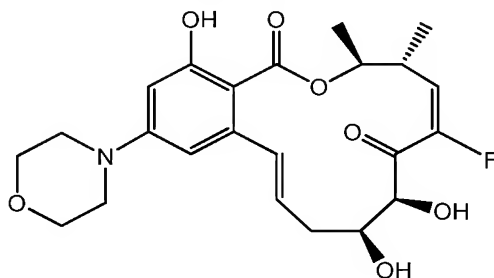
or a pharmaceutically acceptable salt or ester thereof.

99. (new) The composition of claim 88, wherein the compound has the structure:



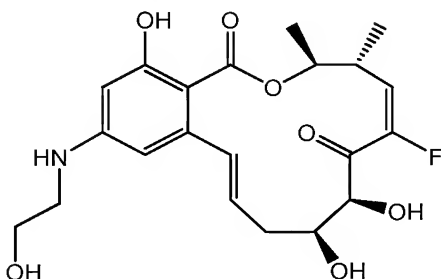
or a pharmaceutically acceptable salt or ester thereof.

100. (new) The composition of claim 88, wherein the compound has the structure:



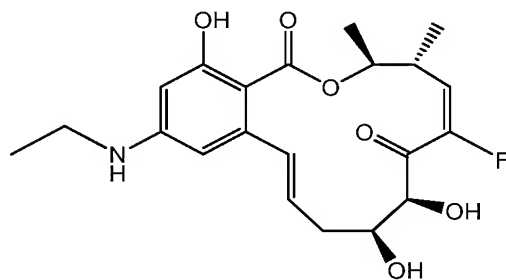
or a pharmaceutically acceptable salt or ester thereof.

101. (new) The composition of claim 88, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

102. (new) The composition of claim 88, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

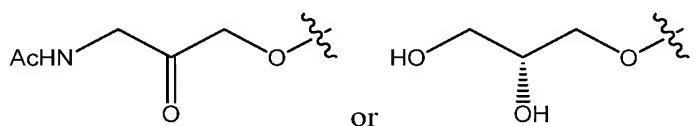
103. (new) The composition of claim 76, where R_1 is hydrogen.

104. (new) The composition of claim 75, where R_3 is halogen.

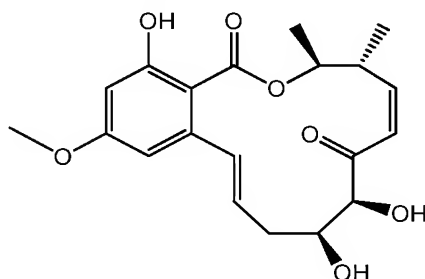
105. (new) The composition of claim 76, where R_4 is hydrogen.

106. (new) The composition of claim 76, where R_5 is hydrogen.

107. (new) The composition of claim 76, where R_6 is hydroxyl.
108. (new) The composition of claim 75, where R_8 is halogen.
109. (new) The composition of claim 76, where R_9 is hydroxyl, protected hydroxyl, $-OR_{12}$, $-NR_{12}R_{13}$, or $-O(CH_2)_pX_2-R_{14}$, wherein R_{12} , R_{13} , R_{14} and X_2 are as defined in claim 76.
110. (new) The composition of claim 109, where R_9 is $-OR_{12}$, wherein R_{12} is methyl, ethyl, propyl, isopropyl, butyl, Bn, PMB (MPM), 3,4-ClBn, or R_9 is

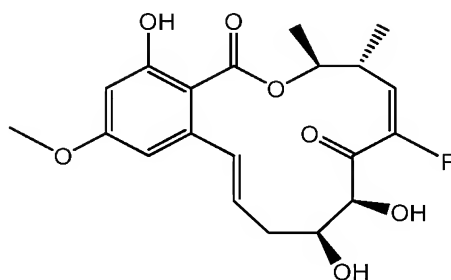


111. (new) The composition of claim 75 wherein the compound has the structure:



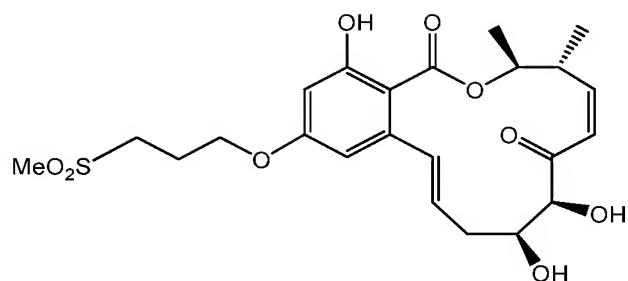
or a pharmaceutically acceptable salt or ester thereof.

112. (new) The composition of claim 75 wherein the compound has the structure:



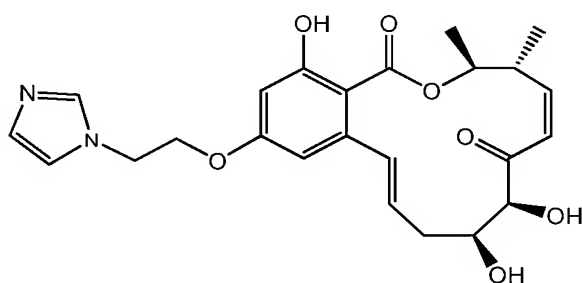
or a pharmaceutically acceptable salt or ester thereof.

113. (new) The composition of claim 75 wherein the compound has the structure:



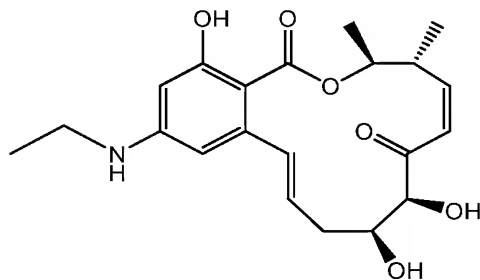
or a pharmaceutically acceptable salt or ester thereof.

114. (new) The composition of claim 75 wherein the compound has the structure:



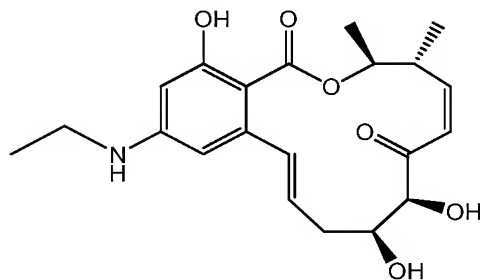
or a pharmaceutically acceptable salt or ester thereof.

115. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:

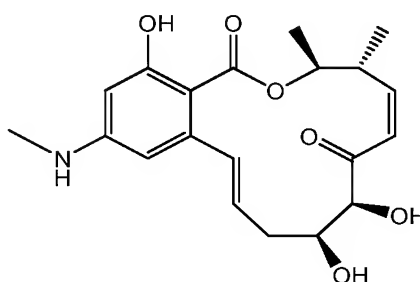


or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

116. (new) The composition of claim 115, having the structure:

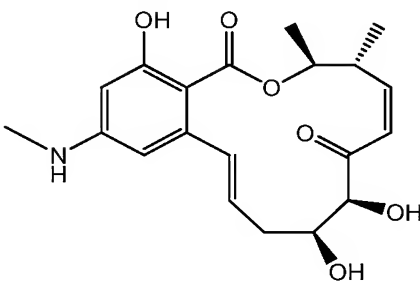


117. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

118. (new) The composition of claim 117, having the structure:



119. (new) The composition of claim 76, wherein R_4 , R_5 and R_8 are hydrogen, R_6 and R_{10} are hydroxyl, and Y and Z together represent trans -CH=CH-.
120. (new) The composition of claim 119, wherein R_1 is methyl.
121. (new) The composition of claim 88, wherein R_4 , R_5 and R_8 are hydrogen, R_6 and R_{10} are hydroxyl, and Y and Z together represent trans -CH=CH-.
122. (new) The composition of claim 121, wherein R_1 is methyl.